Peer Review File

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Reviewer A:

Comment 1: The main purpose of this article is to apply meta-analysis to confirm the correlation between low-expression miR-193b and high cancer metastasis in Asian patients. **Since the linkage of microRNA-related gene networks needs to be carefully demonstrated, meta-analysis using microRNAs as biomarkers requires a sufficient sample size to support the analysis results. The biggest problem of this research is that the sample size is not enough to make a convincing conclusion.**

Reply 1: We are very grateful for your comments regarding our manuscript *MiR-193b as an effective biomarker in human cancer prognosis for Asian patients: a meta-analysis*. All your suggestions are very important to us, both for composing the manuscript and our further research. We have studied comments carefully and have made corrections which we hope meet with approval.

Firstly, to study the prognostic function of mir-193b, clinical studies directly report the human pathology and molecular expression profile, and provide the most reliable statistical data, while animal experiments still need to be verified in human subjects. Therefore, when this inconsistency occurs, we suggest that strict cohort studies better reflect the actual effect of mir-193b. Therefore, after strict screening, the number of samples included is greatly reduced. Considering that the existing clinical research on mir-193b is only carried out on some human cancers, more research is needed, including the survival analysis of cancer patients with different miR-193b expression levels, in order to get more understanding. However, at present, the sample size we can obtain is limited, which is also a deficiency of our research.

Secondly, TCGA database is a tumor database containing the most comprehensive prognostic information and gene expression. We tried to verify the prognostic value of miR-193b using TCGA public database. However, because the sequencing depth for miRNA is limited in TCGA database, certain miRNAs in the database is not detectable. We analyzed the expression level of miR-193b in 33 kinds of tumors in TCGA (Supplementary text 1). The abundance of miR-193b in most of the samples was quite limited, and miR-193b was indetectable in these tumors. Therefore, we encourage cohort studies that focus on miR-193b to further verify its prognostic value, rather than cohort studies that are conjugated with expression profile statistics with limited precision.

Changes in the text: We have stated these contents in the revised manuscript in line 312-318 and 334-339.

Reviewer B:

Comment 1: In this paper the authors explore a microRNA largely involved in mechanisms such as cell proliferation, in the context of cancer. The authors started from a wide meta-analysis, lishedthan half from PMC, while 95 only were kept. Once the reviews or the insufficient papers were removed 10 were kept eventually, 10 about prognosis and 6 with clinicopathological features mentioned. These studies use a total of 1015 patients.

A major conclusion is that overall, high expression of miR-193 is connected to a worse prognosis, and there is already a large literature on this topic. An interesting issue might be the fact that the association does not seem evident for all cancer subtype; for instance, there does not seem to be an association with Head and Neck Squamous Cell Carcinoma (HNSCC), as published by Jamali and coworkers (PMID=25677760), in a metanalysis that the authors should mention for the sake of discussion.

Reply 1: We would like to thank the reviewer for the detailed description of our manuscript. We would like to thank the reviewer for the suggestion to discuss the article (PMID=25677760). I would like to apologize for missing such an important literature. Although mir-19b is related to the prognosis of some tumors, an article (PMID=25677760) elaborated that the expression of mir-19b in Head and Neck Squamous Cell Carcinoma (HNSCC) has no significant correlation with the survival rate of patients. We found the article cited in this meta-analysis, named, *MicroRNA-193b Enhances Tumor Progression via Down Regulation of Neurofibromin 1,* published by Michelle Lenarduzzi and coworkers. Michelle Lenarduzzi included 26 patients with head and neck squamous cell carcinoma with high expression of mir-19b and 25 patients with low expression of mir-19b, and plotted their Kaplan Meier disease-free survival curve. The results showed that the p value was not significant.

Changes in the text: We have stated these contents in the revised manuscript in line 81-83 and 282-284.

Comment 2:

The statistical methodology is standard to alleviate classical biases in epidemiology, and follows the PRISMA standard checklist.

Overall the paper is well written and analyzes pertinent endpoints thoroughly, beyond mere survival (such as tumor size and metastasis). The conclusion consistently proposes that high levels of mir-193b are correlated to a decreased survival, despite an acknowledged data heterogeneity; interestingly the author tracked one of the studies where blood samples rather than tissue samples were analyzed (Madhavan and coworkers). Another possible source of heterogeneity was Mu et al, with a low sample size (48) compared to the other studies. Removing these two studies led to a Hazard Ratio of 0.45 (0.30-0.69), while several related parameters (NOS scores, various carcinomas, …) were associated consistently.

The systematic analysis of the influence of other factors (gender, ns; tumor size, OR=2.36; metastasis in the lymph nodes OR=3.16, or more distant, OR= 3.59)).

Reply 2: Thank you for your careful description of this manuscript and your positive comments about our manuscript.